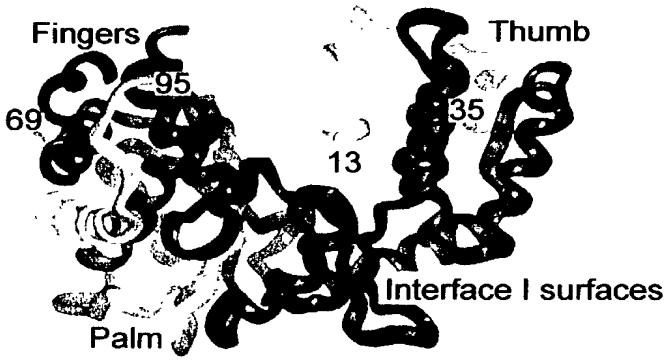
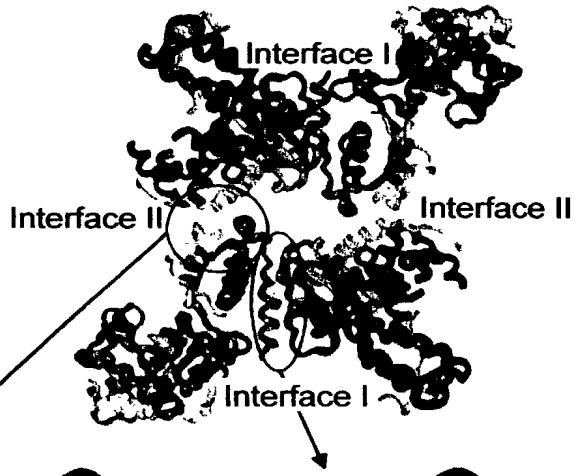


FIG. 1

FIG. 2A



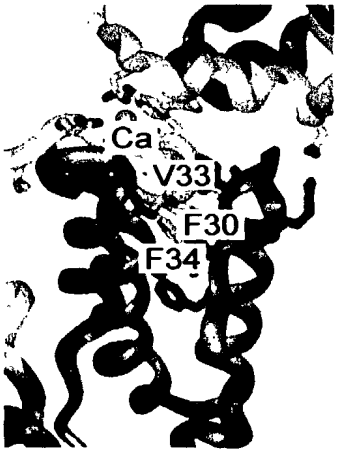


FIG. 2B

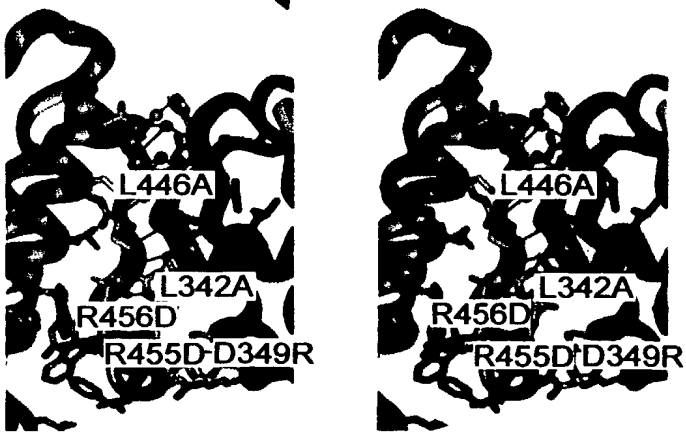
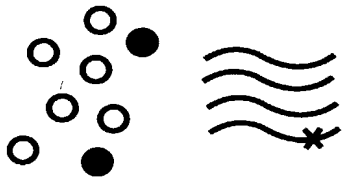


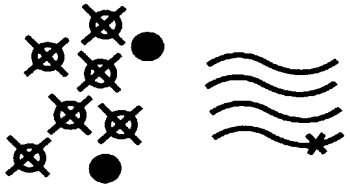
FIG. 2C

A. WHEN THE DRUG TARGET IS MONOMERIC

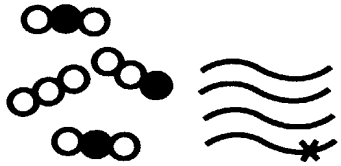


GENETIC: Drug^R mutations will usually be dominant

CONSEQUENCES: Resistant viral progeny are easily selected in presence of drug



B. WHEN THE DRUG TARGET IS OLIGOMERIC



GENETIC: Drug^R mutations will usually be recessive

CONSEQUENCES: Resistant viral progeny are less likely to be selected in presence of drug

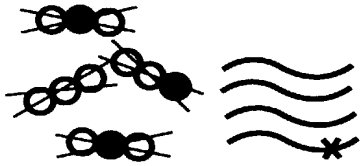


FIG. 3

FIG. 4

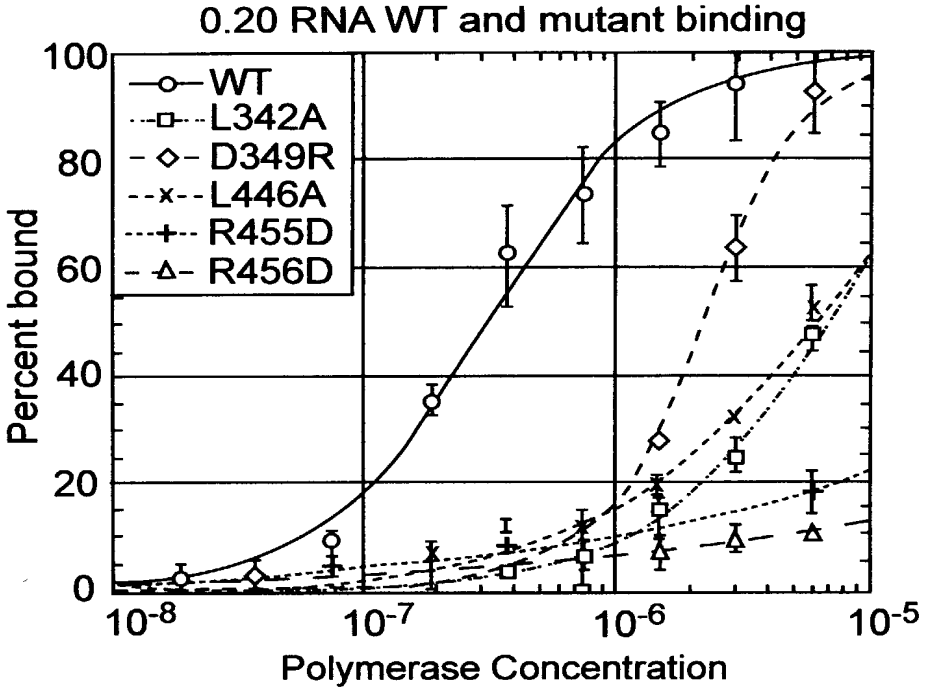

0.20 RNA WT and mutant binding
WT
L342A
D349R
L446A
R455D
R456D
Percent bound
100
80
60
40
20
0
10^{-8}
10^{-7}
10^{-6}
10^{-5}
Polymerase Concentration

FIG. 5

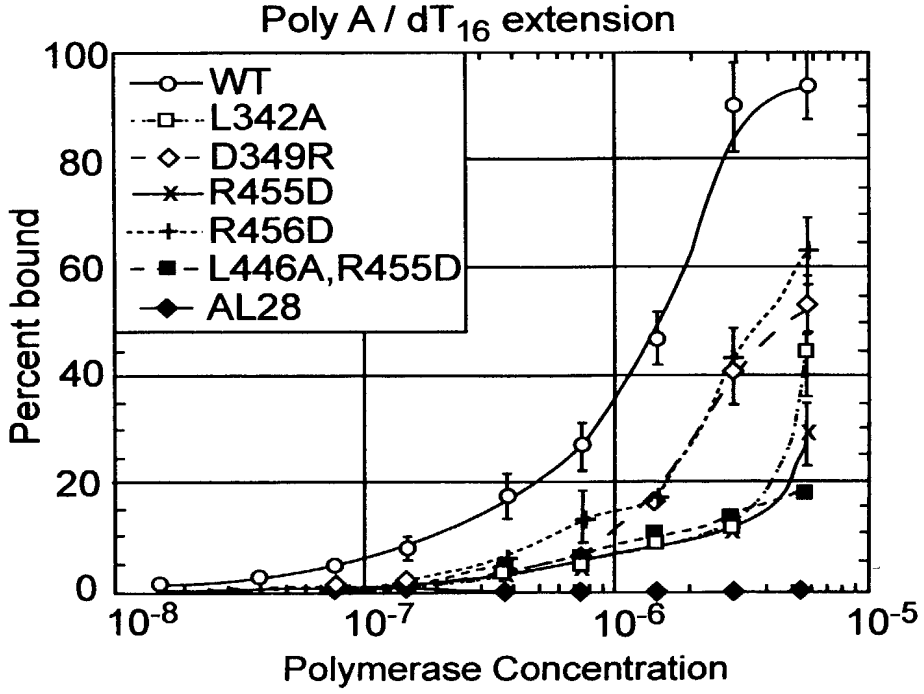

Poly A / dT_{16} extension
WT
L342A
D349R
R455D
R456D
L446A,R455D
AL28
Percent bound
100
80
60
40
20
0
10^{-8}
10^{-7}
10^{-6}
10^{-5}
Polymerase Concentration

FIG. 6

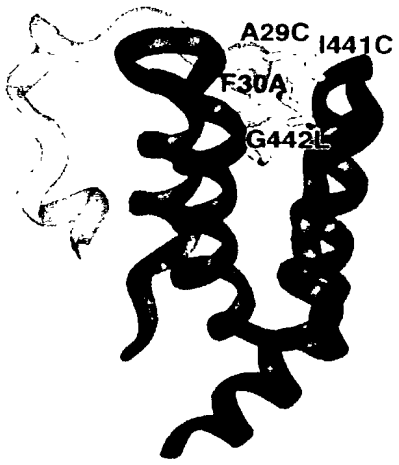


FIG. 7

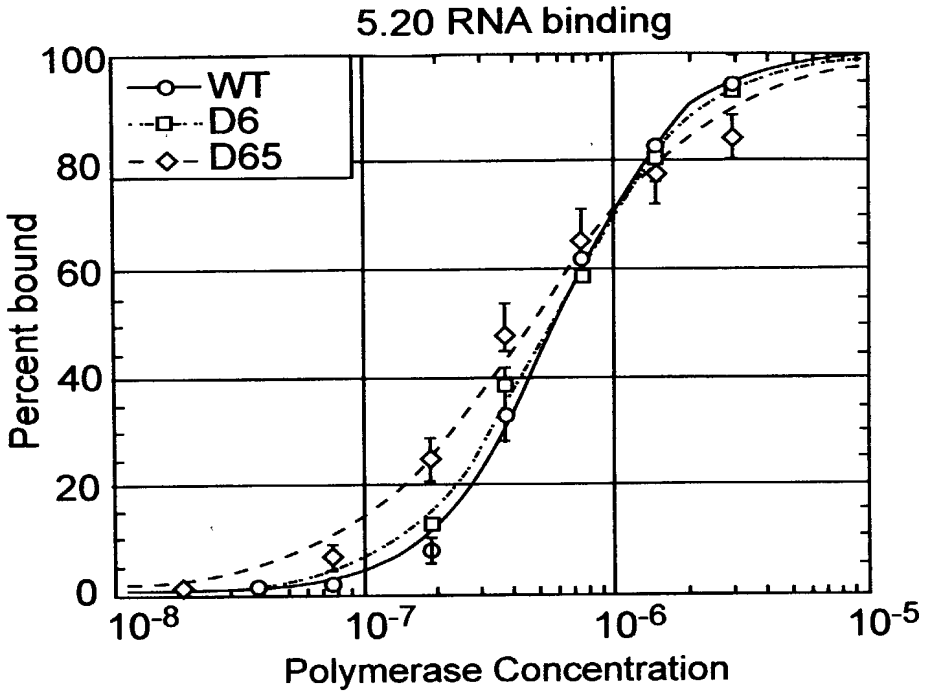

5.20 RNA binding
WT
D6
D65
Percent bound
100
80
60
40
20
0
10^{-8}
10^{-7}
10^{-6}
10^{-5}
Polymerase Concentration

FIG. 8

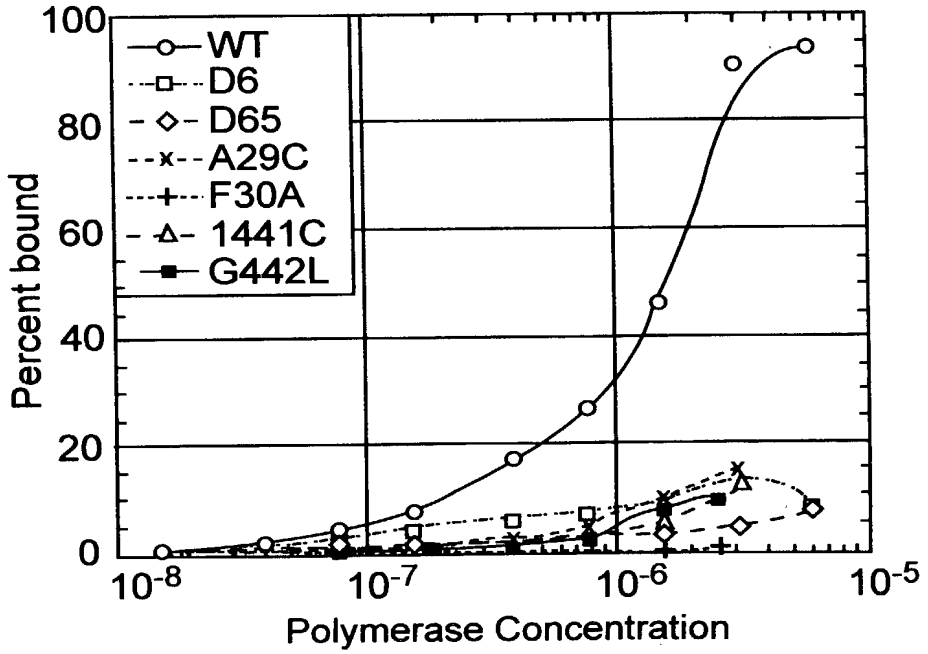

Poly A / dt 16 extension
WT
D6
D65
A29C
F30A
1441C
G442L
Percent bound
100
80
60
40
20
0
10^{-8}
10^{-7}
10^{-6}
10^{-5}
Polymerase Concentration

FIG. 9

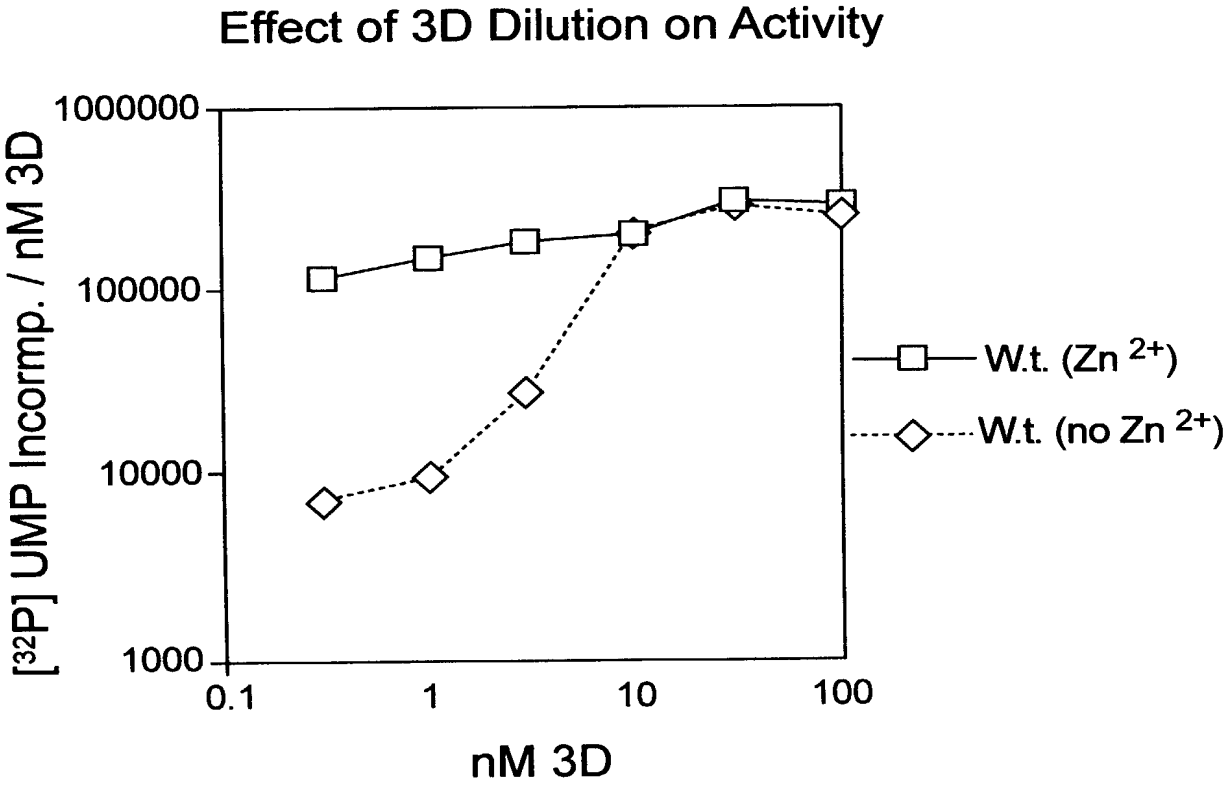

Effect of 3D Dilution on Activity
[32P] UMP Incorp. / nM 3D
1000000
100000
10000
1000
0.1
1
10
100
nM 3D
W.t. (Zn 2+)
W.t. (no Zn 2+)

FIG. 10

Modeling RNA Into the Poliovirus Oligomer

FIG. 11

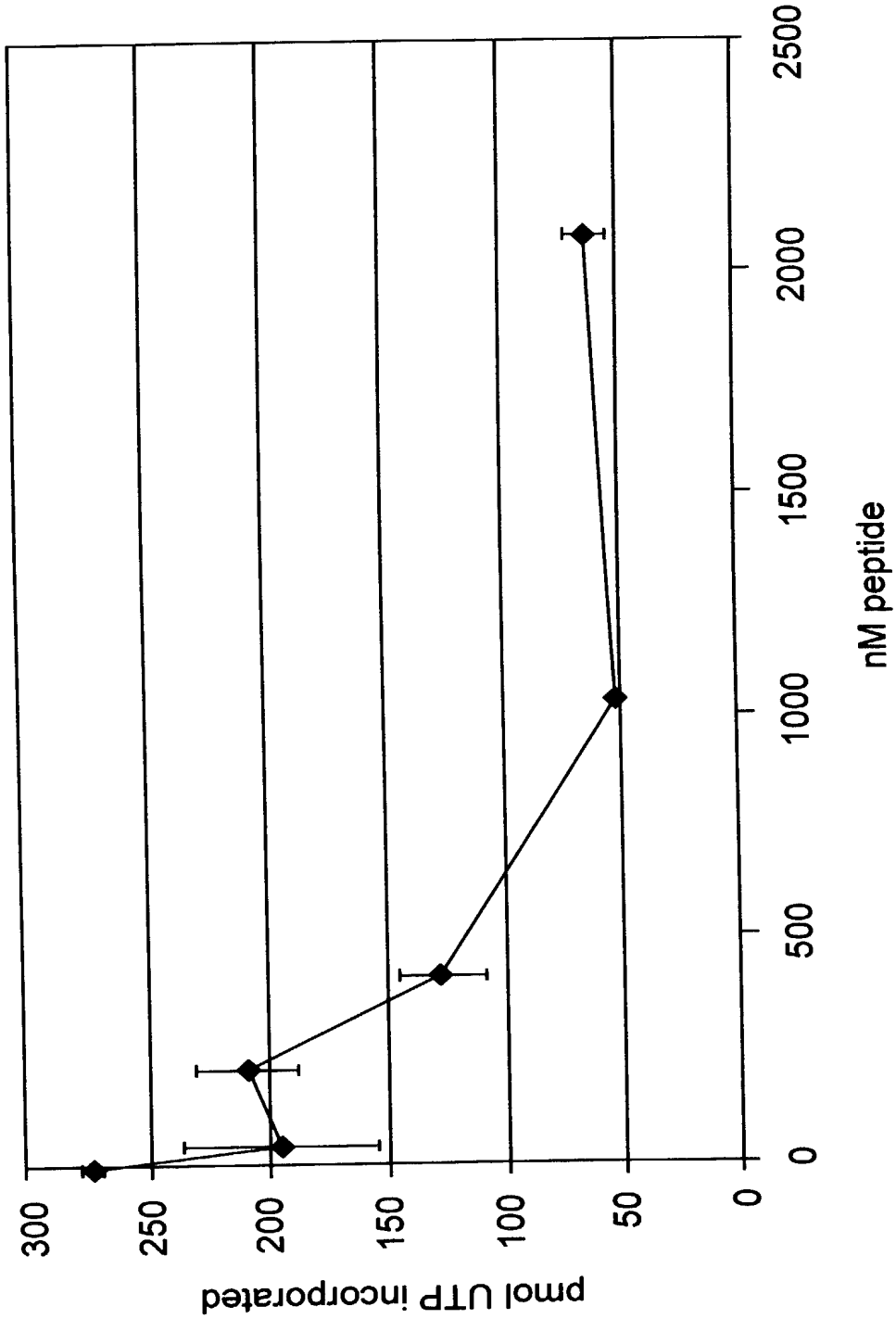


FIG. 12

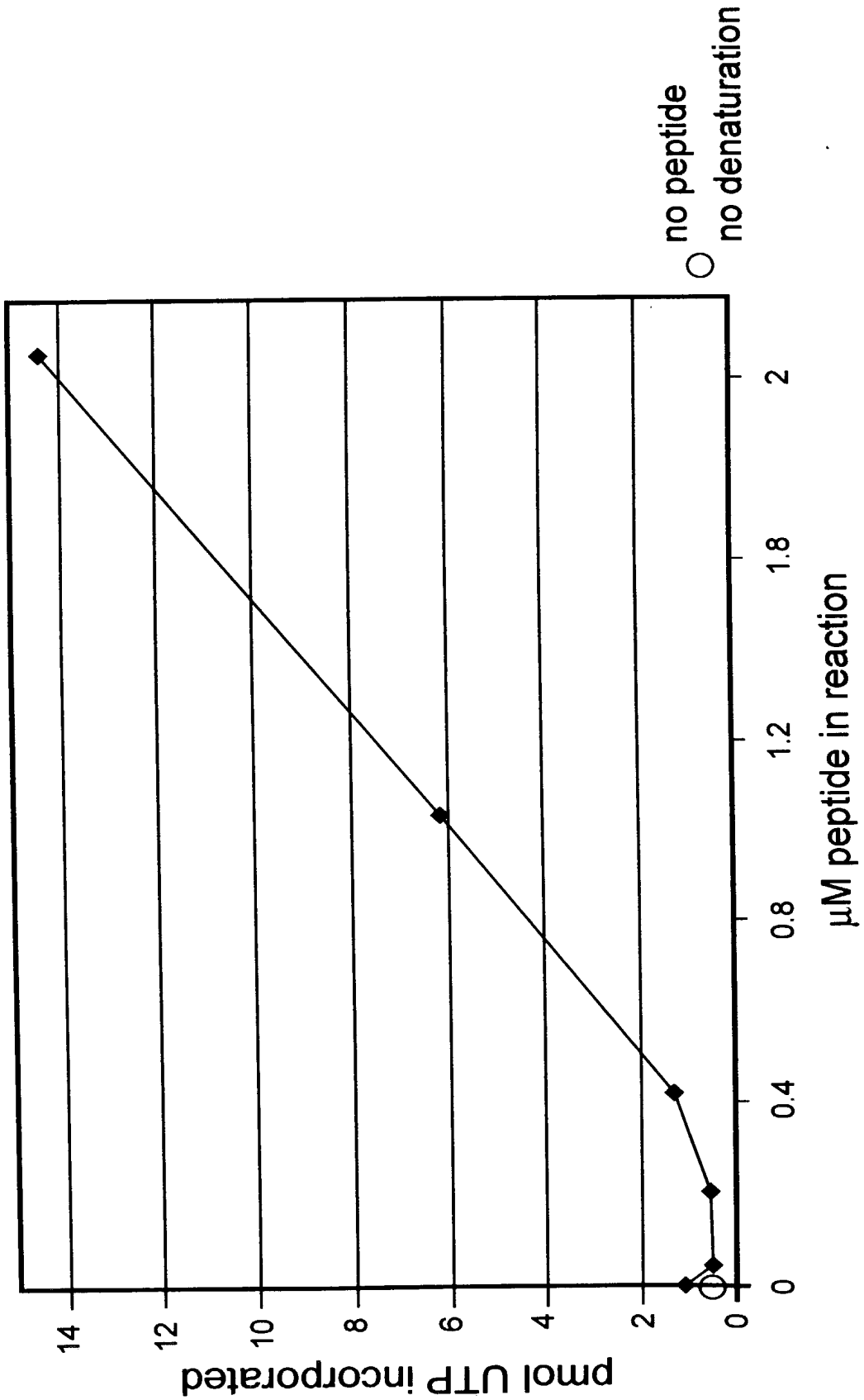
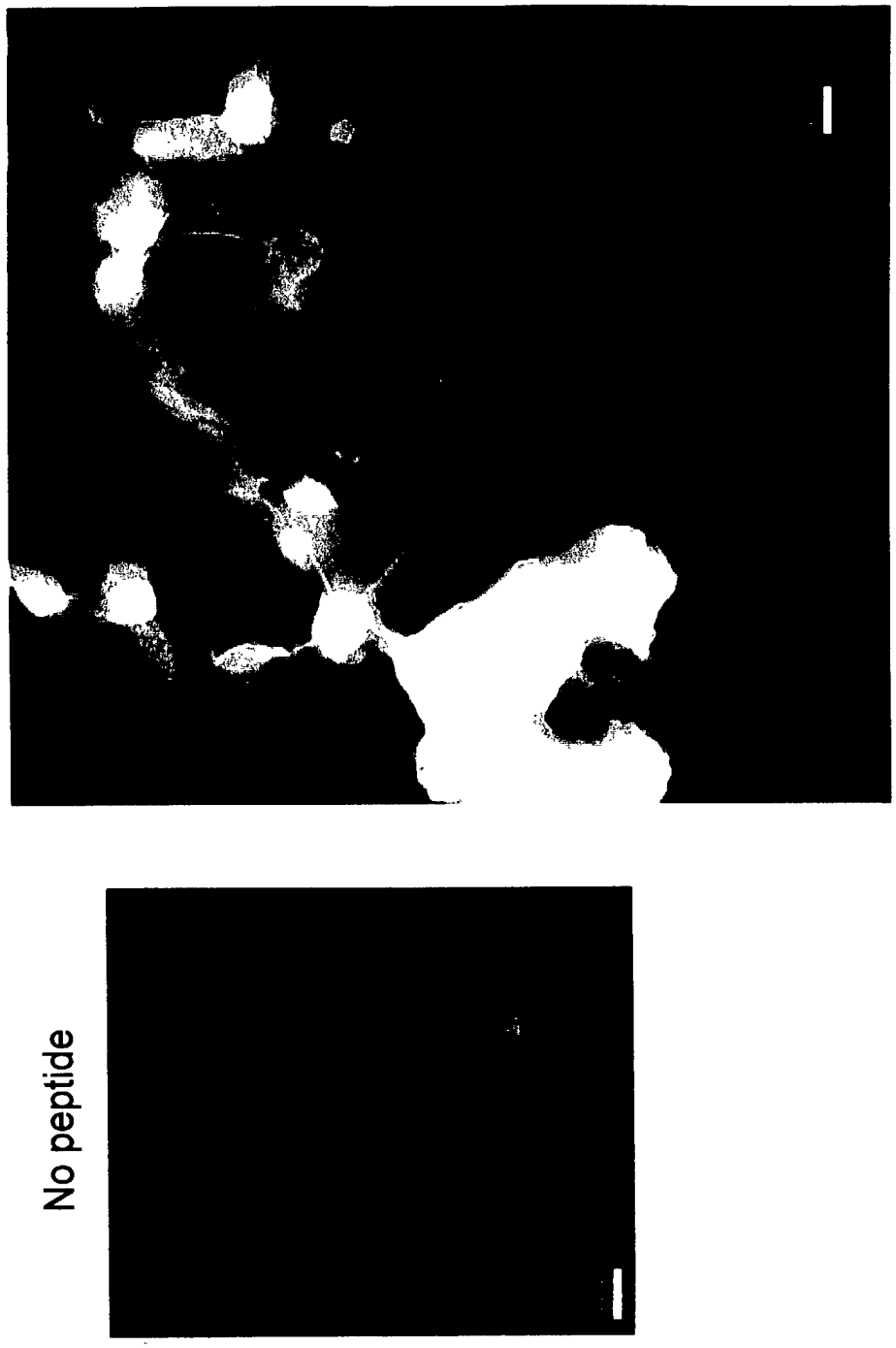

no peptide
no denaturation
pmol UTP incorporated
0
2
4
6
8
10
12
14
0
0.4
0.8
1.2
1.8
2
µM peptide in reaction

FIG. 13



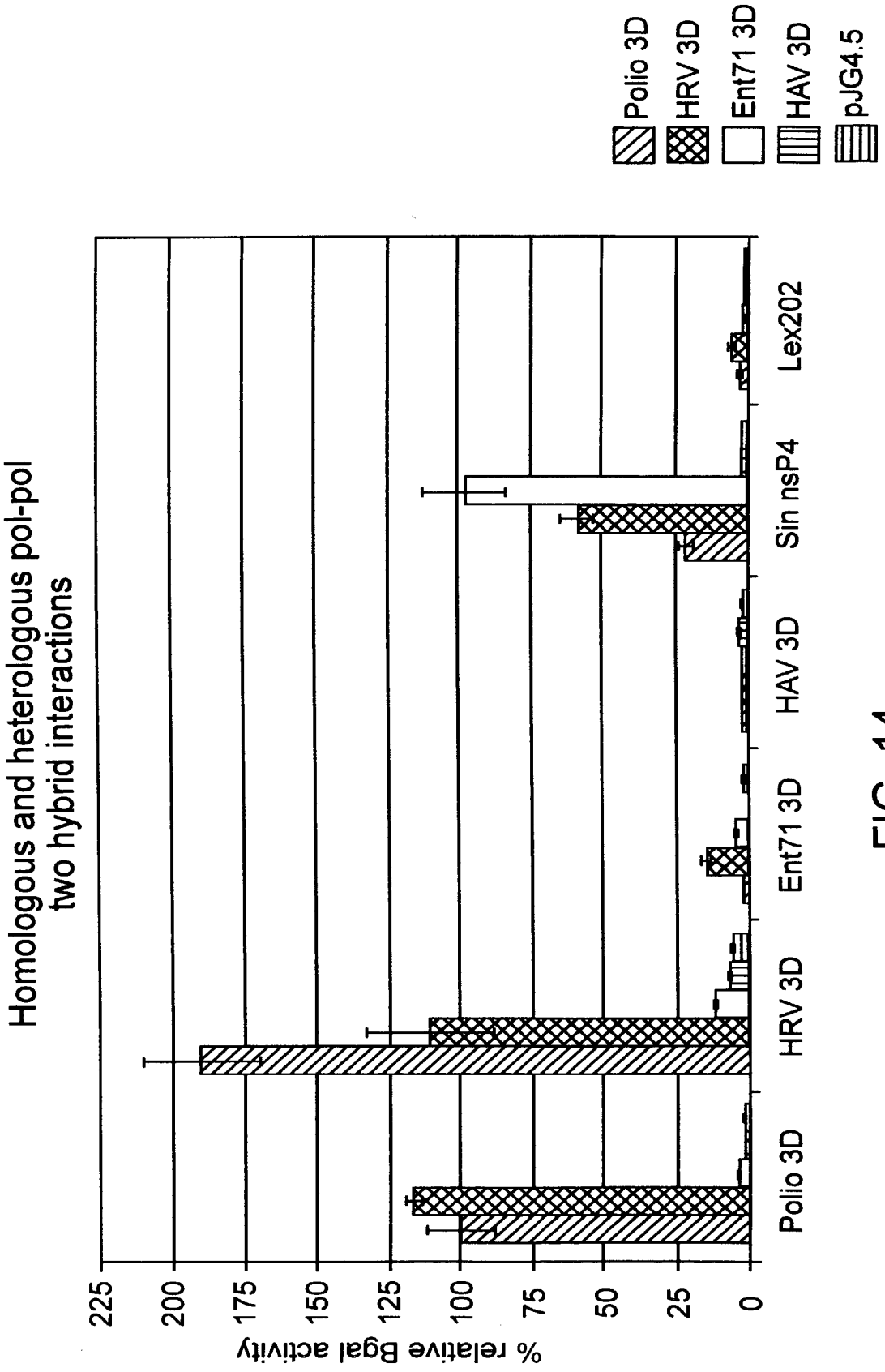
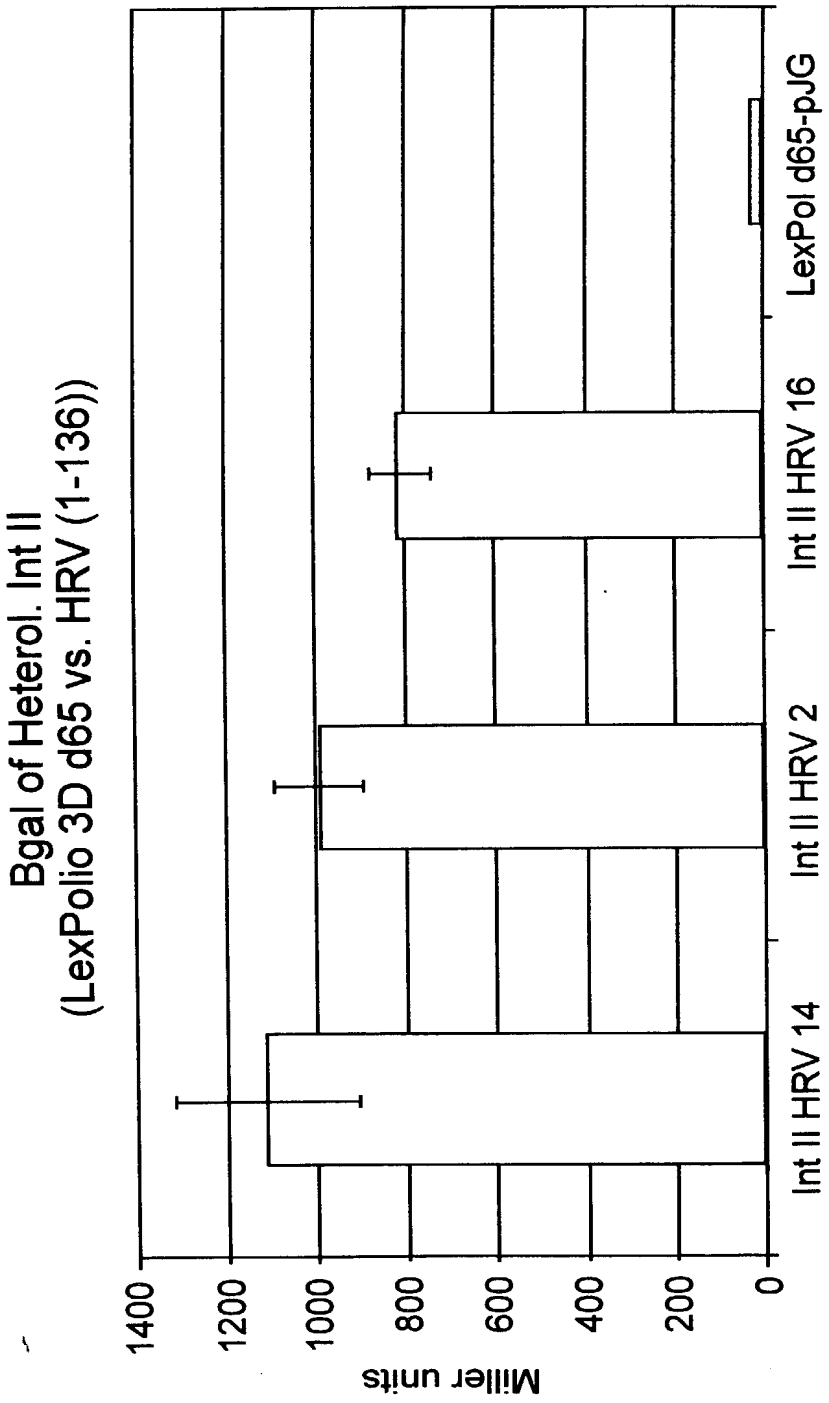

Homologous and heterologous pol-pol
two hybrid interactions
% relative Bgal activity
225
200
175
150
125
100
75
50
25
0
Polio 3D
HRV 3D
Ent71 3D
HAV 3D
Sin nsP4
Lex202
Polio 3D
HRV 3D
Ent71 3D
HAV 3D
pJG4.5

FIG. 14

FIG. 15


Bgal of Heterol. Int II
(LexPolio 3D d65 vs. HRV (1-136))
Miller units
1400
1200
1000
800
600
400
200
0
Int II HRV 14
Int II HRV 2
Int II HRV 16
LexPol d65-pJG